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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,506	08/10/2001	Oxana Ibraghimov-Beskrovnaya	126881201600	8221

7590

11/20/2002

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EXAMINER

HADDAD, MAHER M

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 11/20/2002

11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/830,506

Applicant(s)

IBRAGHIMOV-BESKROVNAYA E
AL.

Examiner

Maheer M. Haddad

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 August 2002 and 03 September 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 1-22, 24-27 and 29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23 and 28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

1. Claims 1-29 are pending.
2. Applicant's election without traverse of Group VIII, claims 23, 28-29 drawn to a method for enhancing cell-cell adhesion in a suitable tissue, comprising an antibody filed on 9/03/02, is acknowledged.
3. A clear and obvious typographical error occurred in the restriction wherein claim 29 which reads on a polycystin Ig-like domain was improperly included in Groups VIII-IX which are drawn to an antibody and a polynucleotide respectively. Therefore claims 29 is drawn to nonelected inventions.
4. Claims 1-22, 24-27 and 29 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.
5. Claims 23 and 28 are under examination as they read on a method for enhancing cell-cell adhesion in a suitable tissue, comprising an antibody.
6. Examiner considers claim 28 was intended to depend from claim 23.
7. The amendment filed 8/13/02 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The preliminary amendment filed on 8-13-02 to the paragraph beginning at line 1 at page 44, substituting "the homophilic binding potential of several Ig-like domains, i.e., Ig^a, Ig^b and Ig^c" with "the homophilic binding potential of several Ig-like a b domains, i.e., Ig^a, Ig^b and Ic^e" represents a departure from the specification and the claims as originally filed. Applicant has not pointed out where the support comes from. However, the specification and the claims as originally filed have no support for the new replacement.

Applicant is required to cancel the new matter in the response to this Office action.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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9. Claims 23 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- A) The term “suitable” recited in claim 23, line 1 and claim 28, line 2 is ambiguous and unclear and the metes and bounds of the claimed “suitable” is not defined.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 23 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for enhancing cell-cell adhesion in a polycystin expressing tissue, comprising delivering to the tissue an antibody against polycystin *in vitro*, does not reasonably provide enablement for a method for **modulating** cell-cell adhesion in any **suitable** tissue, comprising delivering to the tissue **any agent** that **modulates** the binding of polycystin in the tissue, wherein the **modulation** of cell-cell or cell-matrix adhesion is promotion or enhancement of cell-cell or cell-matrix adhesion in a **suitable** cell or tissue. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification disclosure does not enable one skilled in the art to practice the invention without any undue amount of experimentation.

Besides the antibodies to polycystin anti-FP-L1, anti-FP-L2, anti-FP-L3, anti-FP-L4, anti-FP-L5, anti-FP-L6, anti-FP-L7, anti-MAL-REJ, anti-LRR, and anti-BD3, and the homophilic Ig-kike domains Ig^a, Ig^b and Ig^c, the specification fails to provide any guidance as to how to make and how to use any “agent” or any .

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

Applicant has not provided sufficient biochemical information that distinctly identifies such “agents” other than antibodies against polycystin. While any “agent that modulates the binding of polycystin” may have some notion of the activity of the

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“enhancing/inhibiting agent”, claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make such agents, commensurate in scope with the claimed invention. The specification (page 18, lines 9-28) fails to provide any guidance on how to make any antibody, any polycystin domain, any nucleic acid molecule, or any antisense molecule that can be used to enhance a tissue or cell-cell adhesion.

There is insufficient guidance as to which amino acid segments within the polypeptide can be unique and retain a distinct functional capability of the full length polypeptide. *In re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since the amino acid sequence of a polypeptide determined its structural property, predictability of which amino acid fragment can retain the functional capabilities of the full length polypeptide requires knowledge of, and guidance with regard to, which segments in the polypeptide's sequence contribute to its function.

Minor structural differences among structurally related compounds or compositions can result in substantially different biological activities. Therefore, structurally unrelated compounds comprising any “agent that modulates the binding of polycystin” would be expected to have greater differences in their activities.

Therefore, there is insufficient direction or objective evidence as to how to make and to how to use any agent which enhances cell-cell adhesion for the number of possibilities associated with the myriad of direct and indirect effects associated with various “agents” and, in turn, as to whether such a desired effect can be achieved or predicted, as encompassed by the claims.

Also, at issue is whether or not the claimed method would function “*in vivo*”. The specification discloses the addition of GST-Ig^a, GST-Ig^b and GST-Ig^c to MDCK cell monolayers resulted in disruption of cell-cell adhesion. The exemplification is drawn to the disruption of cell-cell adhesion, *in vitro* (pages 57).

In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since no animal was used as model system to enhance cell-cell adhesion. It is not clear that reliance on *in vitro* model to disrupt cell-cell adhesion accurately reflects the relative mammal efficacy of the claimed therapeutic strategy. The specification does not adequately teach how to effectively reach any therapeutic endpoint in mammals by administering the therapeutic the antibody against polycystin. The specification does not teach how to extrapolate data obtained from *in vitro* model of disrupt cell-cell adhesion studies to the development of effective *in vivo* therapeutic treatment, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the antibodies for enhancement of cell-cell adhesion exemplified in the specification.

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The current state of the art in antibody therapeutics and the predictability of treatment efficacy is complicated by the potential for antibody interactions with irrelevant or completing epitopes, Fc region engagement, reduced half life of antibody fragments, and immune response to the therapeutic antibodies (see Ward et al, pages 167-171, 1994 "consideration related to use of blocking antibodies").

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

12. Claims 23 and 28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of a method for enhancing cell-cell adhesion in a polycystin expressing tissue, comprising delivering to the tissue an antibody against polycystin *in vitro*.

Applicant is not in possession of a method for modulating cell-cell adhesion in any suitable tissue, comprising delivering to the tissue any agent that modulates the binding of polycystin in the tissue, wherein the modulation of cell-cell or cell-matrix adhesion is promotion or enhancement of cell-cell or cell-matrix adhesion in a suitable cell or tissue.

Applicant has disclosed only antibodies to polycystin anti-FP-L1, anti-FP-L2, anti-FP-L3, anti-FP-L4, anti-FP-L5, anti-FP-L6, anti-FP-L7, anti-MAL-REJ, anti-LRR, and anti-BD3, and the homophilic Ig-like domains Ig^a, Ig^b and Ig^c; therefore, the skilled artisan cannot envision all the contemplated agents that modulates the binding of polycystin recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such

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identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

13. No claim is allowed.

14. Formal drawings have been submitted which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

15. 1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the “Notice of Allowability.” Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

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All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

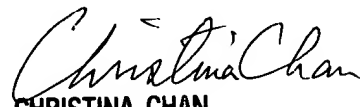
Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
November 18, 2002


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